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Correlation of SARS-CoV-2 RT-PCR cycle threshold with C-reactive protein and clinical outcomes in patients with COVID-19 pneumonitis: A retrospective observational study

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Abstract
Background: SARS-CoV-2 RT-PCR cycle threshold (Ct) values have been proposed as a surrogate for viral burden, while C-reactive protein (CRP) reflects systemic inflammation. Their utility for prognostication in hospitalized patients with COVID-19 pneumonitis remains uncertain.
Methods: This retrospective observational study included 154 adults with symptomatic moderate-to-severe COVID-19 pneumonitis presenting to the Emergency Department of Kokilaben Dhirubhai Ambani Hospital and Medical Research Institute between 1 March 2020 and 15 March 2021. Demographic variables, symptom duration, oxygen saturation, CRP, Ct value, comorbidities, ICU duration, duration of mechanical ventilation, and outcome were analyzed. The median Ct value of 22 was used to compare outcome groups, and correlations were assessed using Pearson correlation and appropriate comparative statistical tests.
Results: The mean age was 60.4 years and 69% of patients were male. The mean CRP was 12.71 mg/dL and mean Ct value was 22.51 ± 4.30. ICU admission was required in 148 patients; 62 required intubation and 46 patients died. Ct value was not significantly associated with ICU duration (p =0.27), need for intubation (p =0.39), duration of intubation (p =0.96), or mortality (p =0.67). No significant correlation was observed between CRP and Ct value in the overall cohort (r=-0.0377, p =0.64), among patients with symptoms >5 days (r=0.019, p =0.864), or among patients requiring ICU admission (r=-0.0626, p =0.61). Multiple comorbidities were associated with significantly higher ICU duration, ventilator duration, and mortality.
Conclusion: In this cohort of hospitalized adults with COVID-19 pneumonitis, a single RT-PCR Ct value did not provide useful prognostic discrimination for ICU stay, intubation, or mortality and did not correlate with CRP. Prognostication should therefore rely on the overall clinical picture and established clinical and biochemical parameters rather than Ct value alone.

Keywords: COVID-19, SARS-CoV-2, RT-PCR, cycle threshold, Ct value, C-reactive protein, CRP, prognostication, pneumonitis, mortality

Introduction
Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), produces a broad spectrum of illness ranging from mild respiratory symptoms to severe pneumonitis, respiratory failure and death. During the early phases of the pandemic, RT-PCR became the principal laboratory method for confirming SARS-CoV-2 infection. The cycle threshold (Ct) is the number of amplification cycles required for the fluorescent signal to cross a predefined threshold and is inversely related to the amount of target nucleic acid in a specimen. [1–8]

Because lower Ct values generally indicate a greater quantity of viral RNA in the tested specimen, Ct values were investigated as potential markers of infectivity and disease severity. However, Ct values are influenced by specimen type, sampling technique, timing of collection, viral kinetics, extraction and amplification procedures, assay design, and reporting methodology. Consequently, a Ct value should not be regarded as a direct and universally comparable measure of viral load. [7, 8, 19–21, 31–38]

C-reactive protein (CRP) is an inflammatory biomarker that has been associated with disease severity and pulmonary involvement in COVID-19. Several studies have reported relationships between viral RNA burden and inflammatory or biochemical markers, although findings have not been consistent across populations and assays. [48–54] The present study was therefore undertaken to examine whether RT-PCR Ct value correlates with CRP and whether Ct value is useful for prognostication among adults hospitalized with COVID-19 pneumonitis.

The study was a retrospective observational analysis conducted at Kokilaben Dhirubhai Ambani Hospital and Medical Research Institute, Mumbai. Adults with symptomatic moderate-to-severe COVID-19 pneumonitis who had documented CRP and Ct values were included. The study period was 1 March 2020 to 15 March 2021, and 154 patients were included in the final analysis. Variables collected included age, sex, symptom duration, oxygen saturation, CRP, Ct value, comorbidities, ICU stay, duration of mechanical ventilation and eventual outcome. [55]

Study Findings

The study population had a mean age of 60.4 years (median 61.5 years; range 20–90 years); 107 patients (69%) were male. The mean duration of symptoms was 5.86 days. Hypertension was the most common comorbidity (52.59%), followed by diabetes mellitus (38.31%). The mean CRP was 12.71 mg/dL and the mean Ct value was 22.51 ± 4.30 (range 15–36).

Table 1: Baseline characteristics and major outcomes of the study population.

Characteristic	Value
Sample size	154
Age, mean (years)	60.4
Male sex	107 (69%)
Symptom duration, mean (days)	5.86
CRP, mean (mg/dL)	12.71
Ct value, mean ± SD	22.51 ± 4.30
ICU admission	148 (96.1%)
Intubation	62 (40.3%)
Mortality	46 (29.9%)

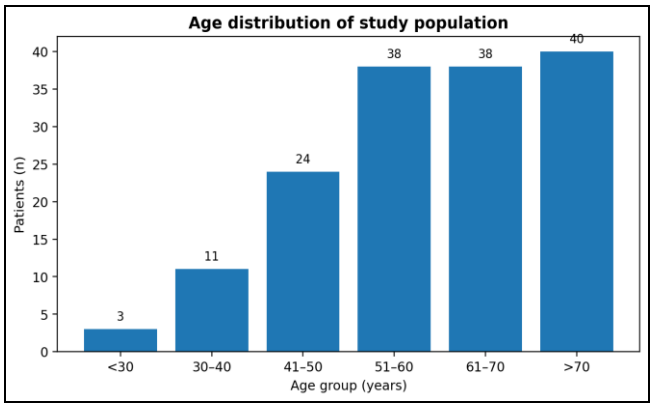

Fig 1: Age distribution of the 154 patients included in the final analysis.

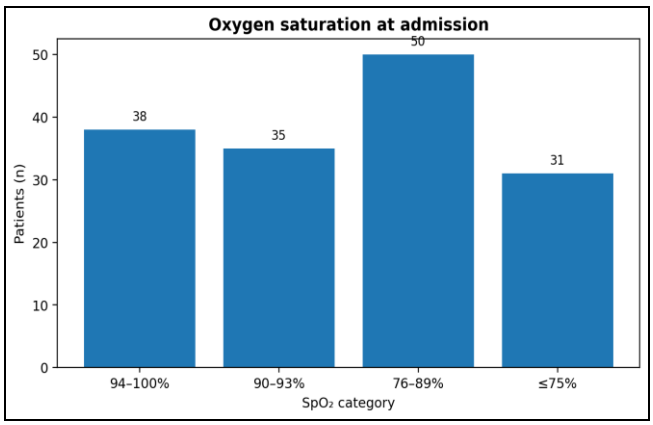

Fig 2: Oxygen saturation distribution at presentation.

The median Ct value was 22 and was used as the principal analytical cut-off. Eighty-one patients had Ct <22 and 73 had Ct >22. ICU duration was 11.87 ± 9.99 days in the Ct <22 group and 13.60 ± 9.44 days in the Ct >22 group (p =0.27). Intubation was required in 30/81 (37.03%) patients with Ct <22 and 32/73 (43.85%) with Ct >22 (p =0.39). Among intubated patients, the mean duration of intubation was 12.5 days and 12.37 days, respectively (p =0.96). Mortality occurred in 23/81 (28.39%) patients with Ct <22 and 23/73 (31.5%) with Ct >22 (p =0.67).

Table 2: Clinical outcomes according to the median Ct-value cut-off of 22.

Outcome	Ct <22 (n=81)	Ct >22 (n=73)	p value
ICU stay, mean days	11.87 ± 9.99	13.60 ± 9.44	0.27
Intubation, n (%)	30 (37.03%)	32 (43.85%)	0.39
Duration of intubation, mean days	12.50	12.37	0.96
Death, n (%)	23 (28.39%)	23 (31.50%)	0.67

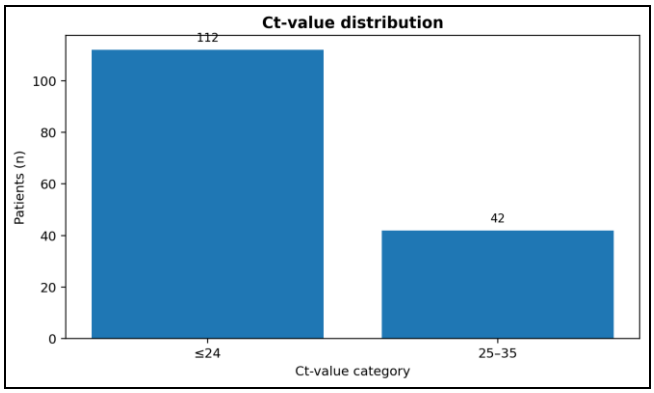

Fig 3: Distribution of Ct values in the study cohort.

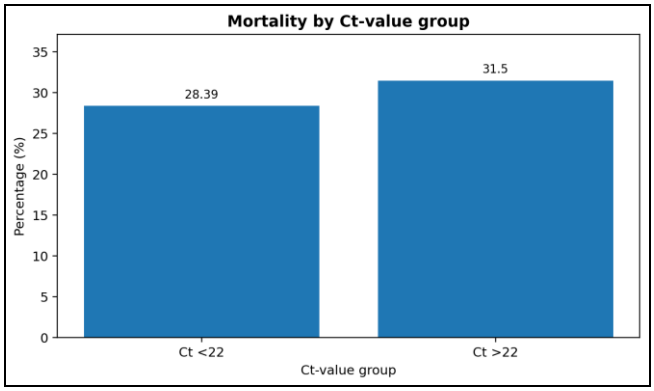

Fig 4: Mortality according to Ct-value group. Difference was not statistically significant (p =0.67).

There was no meaningful correlation between CRP and Ct value in the overall population (Pearson r=-0.0377, p =0.64). Among patients with symptom duration >5 days, the correlation remained negligible (r=0.019, p =0.864). Among those admitted to the ICU, the correlation was also negligible (r=-0.0626, p =0.61). These findings indicate that the Ct value did not track systemic inflammation as measured by CRP in this cohort.

Table 3: Correlation analyses involving Ct value.

Analysis	Pearson r	p value	Interpretation
CRP vs Ct, entire cohort	-0.0377	0.64	No significant correlation
CRP vs Ct, symptoms >5 days	0.019	0.864	No significant correlation
CRP vs Ct, ICU-admitted patients	-0.0626	0.61	No significant correlation
Symptom duration vs Ct, symptoms >5 days	0.6532	<0.00001	Significant positive correlation

An additional analysis among patients with symptom duration >5 days showed a significant positive correlation between symptom duration and Ct value (r=0.6532, p<0.00001), consistent with increasing Ct values as symptoms progressed. However, this did not translate into a

significant association between Ct value and ICU stay, intubation, or mortality.

Comorbidity burden showed a stronger relationship with adverse outcomes than Ct value. Patients with multiple comorbidities had higher mortality (45.76%) than those with a single comorbidity (21.81%) or no comorbidity (17.5%). ICU duration and ventilator duration were also significantly higher in the multiple-comorbidity group, while differences in CRP and Ct values across comorbidity groups were not statistically significant.

Table 4: Outcomes according to comorbidity burden.

Comorbidity burden	CRP (mg/dL)	Ct value	ICU days	Ventilator days	Mortality
None (n=40)	12.11	21.27	9.75	3.25	7/40 (17.5%)
Single (n=55)	11.72	23.03	12.75	4.00	12/55 (21.81%)
Multiple (n=59)	14.06	22.86	14.64	7.11	27/59 (45.76%)

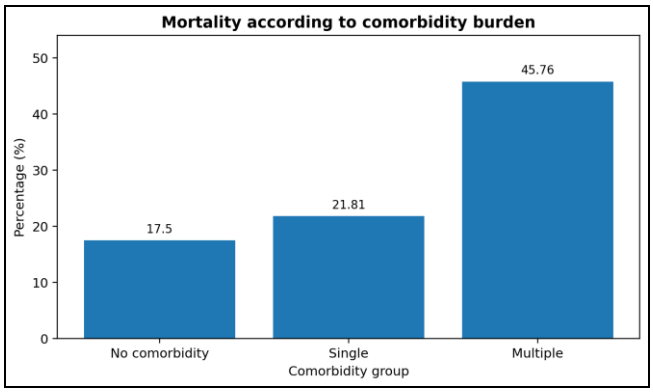

Fig 5: Mortality according to comorbidity burden.

Discussion

The principal finding of this study was that a single SARS-CoV-2 RT-PCR Ct value did not provide useful prognostic information for ICU duration, need for intubation, duration of intubation, or mortality among adults hospitalized with COVID-19 pneumonitis. Similarly, Ct value showed no meaningful correlation with CRP. These findings suggest that Ct value, when interpreted in isolation, should not be used as a surrogate for disease severity in hospitalized patients.

The absence of a CRP–Ct correlation is consistent with the observations of Azzi *et al*., who reported no significant correlation between CRP and Ct value in hospitalized patients with severe COVID-19. Conversely, Liu *et al*. reported an inverse relationship between relative nasopharyngeal RNA load and disease-related parameters, while Shi *et al*. described associations between viral load and serum biomarkers. Differences in specimen type, assay methodology, timing of testing, patient selection and disease stage may contribute to these apparently conflicting observations. [51–53]

Our findings regarding clinical outcomes are also consistent with studies that have questioned the prognostic value of Ct values in hospitalized patients. Arons *et al*. and Kimball *et al*. found no meaningful differences in Ct values across clinical presentation groups, while He *et al*. reported no significant difference in viral-load trajectories between mild/moderate and severe hospitalized patients. In contrast, Huang *et al*. and Yu *et al*. reported associations between lower Ct values and adverse outcomes. Schwierzeck *et al*., in a small pediatric dialysis cohort, also reported lower Ct values in symptomatic than asymptomatic patients. [55–59]

The study also demonstrated a strong relationship between symptom duration and Ct value among patients with symptoms >5 days. This is biologically plausible because viral RNA burden changes over time, and a later sample may have a higher Ct value despite ongoing clinical illness. The finding reinforces the importance of interpreting Ct values in the context of symptom duration and sampling time rather than treating the value as a fixed measure of disease severity. [14, 15, 38]

Multiple comorbidities were associated with substantially higher mortality and longer ICU and ventilator durations. This finding emphasizes that prognosis in hospitalized COVID-19 pneumonitis is multifactorial. Age, baseline respiratory status, comorbidity burden and inflammatory and biochemical markers may have greater practical prognostic relevance than an isolated Ct value. [9, 11, 49, 50]

Several limitations should be considered. The study was retrospective and conducted at a single tertiary-care center, with the inherent limitations of retrospective observational analyses. The analysis focused principally on Ct value and CRP and did not incorporate the full range of hematological and biochemical prognostic markers. Ct values are also assay- and specimen-dependent, and the study period reflected the diagnostic practices of the early pandemic. Therefore, the findings should not be interpreted as evidence that Ct values are universally uninformative; rather, they indicate limited prognostic utility when a single Ct measurement is used in this hospitalized cohort.

Conclusion

In this retrospective cohort of 154 adults with COVID-19 pneumonitis, RT-PCR Ct value was not significantly associated with ICU duration, need for intubation, duration of intubation, or mortality. Ct value also showed no significant correlation with CRP in the overall cohort or in analyses restricted by symptom duration or ICU admission. Although Ct value increased with longer symptom duration among patients with symptoms >5 days, this did not translate into prognostic discrimination. Multiple comorbidities were associated with significantly greater mortality and longer ICU and ventilator requirements. Accordingly, Ct value should not be used alone for prognostication of hospitalized patients with COVID-19 pneumonitis; clinical assessment and established prognostic parameters remain essential.

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